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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/579,032	05/10/2006	Sei Kwang Hahn	HAHN5	3877

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EXAMINER	
LAU, JONATHAN S	

ART UNIT	PAPER NUMBER
1623	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/579,032	HAHN ET AL.	
	Examiner	Art Unit	
	Jonathan S. Lau	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 February 2009 and 06 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-8,11,20,22-27 and 31-36* is/are pending in the application.

4a) Of the above claim(s) *11,20 and 22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-8, 23-27 and 31-36* is/are rejected.

7)☒ Claim(s) *26* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 09 Feb 2009 and 06 Mar 2009 has been entered. Applicant's Amendment, filed 09 Feb 2009, is entered as a matter of right.

This Office Action is responsive to Applicant's Amendment and Remarks, filed 09 Feb 2009, in which claims 1, 2, 9 and 28-30 are canceled, new claims 31-36 are added, and claims 4-7 and 24 are amended to change dependency.

This application is the national stage entry of PCT/JP04/16948, filed 15 Nov 2004; and claims benefit of foreign priority documents JAPAN 2003-385054, filed 14 Nov 2003; JAPAN 2003-407681, filed 05 Dec 2003; and JAPAN 2004-259157, filed 07 Sep 2004; currently an English language translation of these foreign priority documents have not been filed.

Claims 4-8, 11, 20, 22-27 and 31-36 are pending in the current application. Claims 11, 20 and 22, drawn to non-elected species, are withdrawn. Claims 4-8, 23-27 and 31-36 are examined on the merits herein.

Rejections Withdrawn

Applicant's Amendment, filed 09 Feb 2009, with respect to Amended Claims 1, 2, 4-8 and 23-30 rejected under 35 U.S.C. 103(a) as being unpatentable over Yamamoto et al. (US Patent Application Publication 2003/0211166, published 13 Nov 2003, of record) in view of Schense et al. (US Patent Application Publication 2003/0012818, 16 Jan 2003, of record) has been fully considered and is persuasive, as claims 1, 2 and 28-30 are canceled and claims 4-7 and 24 are amended to change dependency. Claims 8, 23 and 25-28 depend from claims 4-7 and 24 and incorporate all limitations therein, including changes in dependency.

This rejection has been **withdrawn**.

Applicant's Amendment, filed 09 Feb 2009, with respect to Amended Claims 1, 2, 4-8 and 23-30 rejected under 35 U.S.C. 103(a) as being unpatentable over Illum et al. (US Patent Application Publication 2001/000765, published 12 Jul 2001, provided by Applicant in IDS filed 10 May 2006) in view of Hubbell et al. (US Patent Application Publication 2002/0177680, published 28 Nov 2002, of record) has been fully considered and is persuasive, as claims 1, 2 and 28-30 are canceled and claims 4-7 and 24 are

amended to change dependency. Claims 8, 23 and 25-28 depend from claims 4-7 and 24 and incorporate all limitations therein, including changes in dependency.

This rejection has been **withdrawn**.

Claim Objections

Claim 26 is objected to because of the following informalities: claim 26 at line 3 appears to misspell drug as "dug". Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Amended Claims 4-8, 23-27 and 31-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yamamoto et al. (US Patent Application Publication 2003/0211166, published 13 Nov 2003, of record) in view of Schense et al. (US Patent Application Publication 2003/0012818, 16 Jan 2003, of record) and further in view of Shu et al. (Biomacromolecules, 2002, 3, p1304-1311, cited in PTO-892).

Yamamoto et al. teaches microspheres of hyaluronic acid to deliver a drug or active substance (page 2, paragraphs 27 and 28). Yamamoto et al. teaches the microspheres prepared by standard spray drying techniques, in which a solution containing the hyaluronate polymer is dispersed to form atomized, or microparticulate, droplets which condense and dry, concentrating the solution (page 2, paragraph 29). Yamamoto et al. teaches chemical cross-linking of the microspheres co-formulated into the microspheres, added to the starting hyaluronic acid starting material or after fabrication in the partially hydrated state (page 2, paragraph 30). Yamamoto et al. teaches using a starting solution containing 0.5% concentration HA, a dilute solution (page 3, paragraph 37). Yamamoto et al. teaches the method wherein said dilute solution contains the crosslinking agent prior to dispersing the solution by spraying (page 4, paragraphs 43 and 44). Yamamoto et al. teaches the process wherein the microspheres made have a diameter between 0.01 and 100 microns (page 2, paragraph 28). Yamamoto et al. teaches the process wherein the microspheres are capable of providing a sustained drug delivery effect (page 3, paragraph 36). Yamamoto et al. teaches drugs or other active agents encapsulated in the microsphere to provide local drug delivery (page 3, paragraph 35). Yamamoto et al. teaches the microspheres are

crosslinked to increase biodegradation time in-situ (page 2, paragraph 28), and one of skill in the art would readily understand biodegradation to involve enzymatic degradation. Yamamoto et al. teaches microspheres so made are injectable (page 4, examples 4 and 5 at right column).

Yamamoto et al. does not teach the specific method wherein the polysaccharide comprises at least one unit represented by Formula I or at least one unit represented by Formula II or the specific crosslinking reaction is a reaction in which crosslinkages are formed by addition reaction between a mercapto group and an unsaturated C-C bond (instant claim 31). Yamamoto et al. does not teach the specific method wherein the dilute solution before the crosslinking reaction contains a drug, and the drug is held in the microparticles obtained after the crosslinking reaction (instant claims 7, 26 and 30). Yamamoto et al. does not teach the specific method wherein the crosslinking reaction does not cause drug denaturation even in the presence of the drug (instant claims 8 and 27). Yamamoto et al. does not teach the specific method wherein the drug is a protein (instant claim 33). Yamamoto et al. does not teach the specific method wherein the sustained release period of the carrier is 24 hours or more (instant claim 34), which is interpreted as an intended use of the product made by the instantly claimed method of making. Yamamoto et al. does not teach the specific method wherein the sustained release period of the carrier is 5 days or more (instant claim 35), which is interpreted as an intended use of the product made by the instantly claimed method of making.

Schense et al. teaches bioactive molecules entrapped within a matrix for the controlled delivery of said bioactive molecules wherein said bioactive molecules are

exntrapped during gelation of the matrix (page 1, paragraph 12). Schense et al. teaches the bioactive molecules include proteins such as growth factors, peptides and enzymes (page 4, paragraph 54). Schense et al. teaches the matrix formed by the reaction of a multi-thiol, or mercapto groups, and a conjugated unsaturated group in a solution that contains a bioactive molecule, or drug, mixed together to perform the crosslinking reaction (page 6, paragraphs 81 and 82). Schense et al. defines a conjugated unsaturated group to include carbon-carbon bonds (paragraph 25 spanning pages 2 and 3), and a conjugated group necessarily has two or more carbon-carbon double bonds in conjugation. Schense et al. teaches the matrix-forming reaction is self-selective, meaning the thiol preferentially reacts with the conjugated unsaturated group rather than other biological compounds such as the bioactive molecule, indicating that the matrix-forming reaction does not cause drug denaturation (page 3, paragraphs 26 and 27). Schense et al. does not explicitly describe the gelation or matrix-forming reaction as a crosslinking reaction, however one of ordinary skill in the art would understand the terms gelation and matrix as described in page 3 paragraphs 29 and 30 to refer to the formation of a crosslinked polymer. Schense et al. teaches the matrix made of natural polymers such as hyaluronic acid (page 3, paragraph 39). Schense et al. teaches a matrix wherein the bioactive molecule is released completely within several weeks (page 7, paragraph 85), teaching that the product is capable of being used in an intended use such that the sustained release period of the carrier is 5 days or more.

Yamamoto et al. in view of Schense et al. does not specifically teach the specific method wherein the polysaccharide comprises at least one unit represented by Formula I or at least one unit represented by Formula II.

Shu et al. teaches thiol-modified hyaluronic acids used in crosslinking to slow down degradation are known for the purpose of in the field of drug delivery (page 1304, abstract, left column paragraph 2 and right column paragraph 1). Shu et al. teaches a thiol-modified hyaluronic acids having the structure having a thiol reading upon instant Formula I (page 1306, figure 2 at top of page).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine Yamamoto et al. in view of Schense et al. and further in view of Shu et al. All of Yamamoto et al., Schense et al. and Shu et al. are drawn to crosslinked hyaluronic acid for sustained release of a bioactive molecule. One of ordinary skill in the art at the time of the invention would be motivated to combine the invention of Yamamoto et al. in view of Schense et al. to improve a similar product and process in the same way because Schense et al. teaches the improvement increases the retainable concentration of bioactive molecules in a matrix (Schense et al. page 1, paragraph 9). It would have been obvious to substituted the thiol-modified hyaluronic acids taught by Shu et al. for the thiol-modified hyaluronic acids taught by Schense et al. because both thiol-modified hyaluronic acids are known for the same purpose of forming crosslinked hyaluronic acids to slow down degradation in the field of drug delivery.

Response to Applicant's Remarks:

Applicant's Remarks, filed 09 Feb 2009, with regard to Yamamoto et al. in view of Schense et al. have been fully considered and not found to be persuasive.

Applicant states that Yamamoto et al. is drawn the crosslinking reaction after formation of the microspheres and therefore does not meet the limitations of the instantly claimed method wherein the crosslinking agent is present prior to dispersing the solution by spraying and the crosslinking reaction occurs during concentration of the solution contained in the droplets formed by said spraying. However, Yamamoto et al. teaches the method wherein said dilute solution contains the crosslinking agent prior to dispersing the solution by spraying (page 4, paragraphs 43 and 44).

Applicant notes that Yamamoto et al. teaches crosslinking of the microspheres after fabrication in Example 3 at page 4, said microspheres made according to the method of Example 2 as cited in page 4, paragraphs 43 and 44. However, the broader teaching of Yamamoto et al. encompasses both the microspheres made according to the method of Example 2, wherein the method includes the dilute solution containing the crosslinking agent prior to dispersing the solution by spraying, and the microspheres made according to the method of Example 3 cited by Applicant. Yamamoto et al. teaches in Example 4 at page 4, paragraphs 49-50 and in Example 5 at page 4, paragraphs 51-52 that the microspheres fabricated according to Example 2 is useful for the same purpose as the microspheres fabricated according to Example 3. While the post fabrication crosslinking in Example 3 may increase the stabilization of the microspheres (page 4, paragraph 47) a known or obvious composition does not become patentable simply because it has been described as somewhat inferior, or not

additionally improved, to some other product for the same use. Accordingly, the broader disclosure of Yamamoto et al. is found to teach the method wherein the dilute solution contains the crosslinking agent prior to dispersing the solution by spraying.

Conclusion

No claim is found to be allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jonathan S. Lau whose telephone number is 571-270-3531. The examiner can normally be reached on Monday - Thursday, 9 am - 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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